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The Acute Effect of Environmental Tobacco Smoke Exposure on Asthmatics: Studies with a Dynamic Challenge Chamber

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Abstract To determine the acute effects of environmental tobacco smoke on respiratory tract lung function, 130 asthmatics and 28 non-asthmatics were exposed up to 4 hours to side stream environmental tobacco smoke (SS-ETS) in a dynamic challenge chamber. The vast majority of the subjects exposed to SS-ETS reported upper respiratory and ocular irritant symptoms; the prevalence of these symptoms was not significantly associated with any particular study groups analyzed, or with the self-perception of tobacco smoke allergy by the study subject. All 28 SS-ETS-exposed non-asthmatics had no significant change in lung function, while 26/130 asthmatics demonstrated a significant drop in pulmonary function (FEV_1 ≥20% decline), generally within 90 to 240 minutes after start of exposure. Classical late phase bronchoconstriction was not observed up to 24 hours following the challenge. Six/26 reactors had a significant drop in lung function following a sham control challenge, indicating that 20/130 asthmatics had a specific bronchoconstrictive response to SS-ETS. Responses to diminishing levels of SS-ETS demonstrated that some asthmatics can react to levels as low as 0.0128 cigarette – min/m^3 (comparable to ETS levels in the homes of many smokers).

Key words Cigarettes; Environmental Tobacco Smoke; Dynamic Exposure Chamber; Respiratory Tract; Lung Function; Asthmatics.

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Background

As recent as 1990, it has been estimated that approximately 26% of the United States adult population (approximately 50 million Americans) are smokers (Center for Disease Control, 1990); thus, there is a substantial likelihood that many American adults and children are exposed to environmental tobacco smoke (ETS) on a daily basis (Rando et al., 1997). Tobacco smoking has long been recognized as a major source of morbidity and mortality (Public Health Service, 1979). However, only recently have the health effects of ETS on nonsmokers exposed in a passive manner become of concern (Rando et al., 1997; Shepard et al., 1979; Wiedemann et al., 1986; Dahms et al., 1981; Chilmonczyk et al., 1993; Brownson et al., 1992). Because of perceived negative effects about this exposure, there has been a growing concern by the public resulting in the banning of smoking in many public places, such as restaurants, office buildings and stadiums (U.S. Department of Health and Human Services, 1991; Center for Disease Control, 1992).

The public's concern as to the effects of smoke on the nonsmoker has led to the need for more information concerning effects of passive exposure to tobacco smoke of individuals with chronic respiratory diseases such as asthmatics, and the levels of smoke that induce such effects. A number of previous studies (Shepard et al., 1979; Wiedemann et al., 1986; Dahms et al., 1981; Stankus et al., 1988; Menon et al., 1988) investigated bronchial reactivity of asthmatic subjects to ETS in static test atmospheres. Although two studies (Shepard et al., 1979; Wiedemann et al., 1986) did not show a decline in pulmonary function of test subjects after ETS exposure, several others (Shepard et al., 1979; Dahms et al., 1981; Stankus et al., 1988; Menon et al., 1988) have demonstrated a significant decline in forced ex-

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piratory volume in one second (FEV_1) following exposure in some subjects.

The smoke generated by the burning cigarette is divided into mainstream smoke, which the smoker inhales, and sidestream smoke (SS-ETS) emanating from the burning tip of the cigarette. ETS consists of exhaled mainstream smoke and SS-ETS. Other minor components are generated by diffusion through the paper or escape from the filter.

Maintenance of precise ETS levels in a static test chamber is difficult; intra and interchallenge variability in suspended particulate matter, and airborne nicotine levels are observed. Furthermore, most test atmospheres produced in previous studies have been generated with mainstream ETS which differs substantially from SS-ETS. Finally, the particulate counts in a static chamber can decrease during the long time period of challenge, due to surface adsorption, while the gaseous phase accumulates in the test chamber (Stankus et al., 1988). This yields abnormally high carbon monoxide levels in the static chamber. Thus, static chambers do not necessarily reflect the typical smoke atmosphere to which the public is exposed.

To address these issues, a dynamic test chamber was developed to conduct challenge studies under more realistic and more precise conditions with the desired levels of SS-ETS concentrations. The dynamic cigarette smoke inhalation challenge chamber allows very precise control of test atmospheres for as long as necessary by varying the number of cigarettes smoked and adjusting the airflow, to assure accurate levels of SS-ETS, CO, particulate counts, and nicotine (Rando et al., 1992). This chamber enables exposure of study subjects to passive cigarette smoke under real-life conditions. Accordingly, asthmatic and non-asthmatic individuals were exposed to SS-ETS for 4-hour periods in a dynamic test chamber and changes in their lung function, as well as self-perceived irritant symptoms resulting from smoke exposure, were recorded.

Materials and Methods

Subjects

A total of 158 subjects were recruited for the study. Of these, 130 were physician-diagnosed asthmatics (have asthma for greater than 2 years) based on their prior medical history (symptoms of coughing, wheezing, and shortness of breath) and a documented 15% reversibility in their FEV_1 after bronchodilator use (based on the American Thoracic Society criteria for definition of asthma). Non-specific airway hyperreactivity was assessed by methacholine challenge in 92 of the 130 asthmatics. Twenty-eight subjects were non-asthmatics. They were recruited by advertisement in a local newspaper and from the Charity Hospital Allergy Clinics. After obtaining informed consent, each study subject was asked to complete a questionnaire inquiring about his/her perception of pulmonary and extrapulmonary reactions from exposure to environmental tobacco smoke, their use of medications and other pertinent demographic information.

Subjects were grouped into atopics and non-atopics, where atopy was defined as the presence of symptoms of seasonal asthma and/or rhinitis plus positive skin test reactivity to two or more common inhalant allergens. Skin tests were performed using the skin prick method with histamine as positive control and 50% glycerine in PBS as negative control. All subjects were prick skin tested with 25 environmental allergens including house dust, mite, grasses, trees, weeds and molds. After fifteen minutes, the skin test site was read and positive tests were those with a wheal formation of 3 mm or greater compared to the negative control.

Dynamic Inhalation Challenge Chamber

The dynamic cigarette smoke inhalation challenge chamber (2.57×2.49×2.64 meters, volume 16.9 m^3) has been described in detail previously (Rando et al., 1992). It has an antechamber that houses the smoke generation and monitoring devices and spirometer. Smoke is carried into the test chamber through an air diffuser grille in the common wall between the chamber and antechamber. Ventilation of air through the chamber was provided by an exhaust fan installed over the ceiling opposite the common wall between the chamber and antechamber.

The chamber is designed so as to keep the smoke-generating equipment, temperature and humidity monitors, spirometer and the observer isolated from the subject. Intercom and a glass window are also provided for visual observation of the subject and ease of communication between the observer and the subject. The subject has access to various reading and video viewing material in efforts to make the environment as comfortable as possible. The furniture present in the chamber is of non-absorptive material.

Flow rate in the chamber is controlled by a combination of adjustable louvers in the exhaust duct and a 2-speed controller in the blower. Pressure drop across the louvers is monitored and used to confirm chamber flow. The actual flow through the chamber was determined at the dilution air grille of the antechamber with a calibrated flow hood (Shortridge, Instruments Model CFM-83). Based on its volume, the chamber could be ventilated at a rate of 0.1 to 0.7 air changes per minute (Rando et al., 1992).

Cigarette Smoke Generation

Passive cigarette smoke was generated by smoking 1R4F cigarettes (University of Kentucky, Tobacco and Health Research Institute, Lexington, KY) using a fully automatic smoking machine (Heinr Borgwaldt, Hamburg, Germany). One or two 1R4F cigarettes were continuously smoked at a puff volume of 75 ml, 1 puff per minute (8 puffs per cigarette). Main stream ETS was diverted to an exhaust duct for removal and SS-ETS was allowed to flow into the chamber under the action of dilution flow.

Monitoring of ETS Challenge Atmospheres

SS-ETS levels in the test chamber were continuously monitored using a Sibata Model P5 (MDA Scientific, Lincolnshire, IL) aerosol monitor. Samples for airborne nicotine quantitation were collected using XAD-4 resin tubes (SKC Inc., Eighty-four, PA) at a flow rate of one liter/minute and analyzed by gas chromatography. Samples were also collected on pre-weighed Teflon filters for gravimetric analysis, following which the filters were desorbed in methanol and photometric analysis was performed at 325 nm to determine ultraviolet absorbing particulate matter (UVPM). These procedures have been described in detail elsewhere (Rando et al., 1992).

The initial challenge tests were done at SS-ETS levels equivalent to a smoke index of 1.18 cigarette – min/m^3. The smoke index is calculated as the ratio of the number of cigarettes being continuously smoked to the dilution flow rate through the chamber. For this work, a smoke index of 1.18 cigarette – min/m^3 is obtained by smoking 2 cigarettes at a time with a chamber dilution flow rate of 1.7 m^3/min. Selected challenges were conducted at smoke indexes of 0.59, 0.27, 0.128 and 0.093 cigarette min/m^3. These smoke indexes were obtained by varying the number of cigarettes being smoked (1 or 2) and the chamber dilution flow rate (1.7 m^3/min to 10.75 m^3/min.) ETS levels in the chamber were equivalent to that of a smoke-filled bar or restaurant.

Cigarette Smoke Inhalation Challenge Protocol

The study was approved by the Human Experimentation Committee of Tulane University Medical School and all participants gave informed consent prior to commencement of the study. The complete ETS challenge protocol has been published previously (Stankus et al., 1988). All challenges were performed in the General Clinical Research Center (GCRC) inhalation chamber when subjects' asthma was "stable" (FEV_1 ≥70% of predicted) and their medications were withheld as per established guidelines (American Thoracic Society News, 1980). All ETS challenges commenced between 8 and 9 a.m. A temperature of 21°C to 24°C and a relative humidity of 50% to 60% were maintained during the challenge. All subjects underwent a standard 240 minute (min) inhalation challenge to SS-ETS at a smoke index of 1.18 cigarettes – min/m^3 which corresponded to UVPM of 1553±53 μg/m^3, nicotine (NIC) level of 379±13 μg/m^3, and a carbon monoxide level of approximately 12 ppm. Any subject demonstrating a ≥20% fall in FEV_1 (reactors) was allowed to exit the test chamber at the time of "reaction." Reactors were treated appropriately to relieve their bronchospasm. All others (non-reactors) remained in the chamber until completion of the challenge. Any subject requesting termination of the exposure was allowed to exit the chamber at any time – none requested this. Subjects were monitored for up to 24 hours (except when asleep) from the commencement of the challenge with hourly peak flow measurements, using a mini Wright peak flow meter.

All reactors to the SS-ETS challenge were subjected to a sham control challenge for the same duration of the smoke challenge. During the sham challenge, the reactors stayed in the chamber without the presence of cigarette smoke and were tested in the same way as during the standard SS-ETS challenge. A positive reactor is defined as a subject with an FEV_1 drop ≥20% upon SS-ETS exposure, and <20% FEV_1 drop upon sham challenge.

All subjects completed a symptom response sheet, upon completion of the challenge, in which they recorded conjunctival, nasal, pharyngeal or lower respiratory tract symptoms and overall acceptability or unacceptability of the exposure.

Pulmonary Function Tests

Pulmonary functions for each study subject consisted of simple spirometry. FEV_1, FVC, and peak expiration flow rate were determined (at baseline, and at 30 minute intervals thereafter for the duration of the challenge) using a Pulmonaire® (Jones Medical Instrument Co., Oakbrook, IL) Spirometer with a Datamite 3 mi-

Table 1 Demographics of the smoke challenge population

	Asthmatics		Non-asthmatics
	Total	Reactors	
Number	130	26	28
Age range	18–60	19–60	18–50
Mean age	34	36	30.5
Caucasian/black	65/65	13/13	14/14
Male/female	37/93	6/20	8/20
Atopic/non-atopics	112/18	21/5	22/6

croprocessor. Studies were performed in the Tulane-LSU General Clinical Research Center. Triplicate measurements were made and the data expressed as the single best effort of the three determinations for each time interval. In addition, the subjects were taught to use the Mini Wright Peak Flow Meter (MWPFM) for

Table 2 Demographics and lung function changes of ETS challenge reactors[a]

Subject #	Age	Race	Sex	Smoking history	Smoke-induced symptoms	SS-ETS exposure level as cig-min/m^3	
						1.18	0
01	55	W	F	Ex-smoker	Asthma/SOB/wheezing/nasal symptoms	−24/180[b]	Negative
02	34	B	F	Ex-smoker	Asthma/SOB/wheezing/nasal symptom/hives	−30/90	Negative
03	22	W	F	Non-smoker	Asthma/SOB/wheezing	−20/240	Negative
04	34	B	F	Non-smoker	Asthma/SOB/wheezing/nasal sympt/conjunctivitis	−21/30	Negative
05	43	B	F	Not known	Not known	−20/150	Negative
06	41	B	M	Non-smoker	No response	−37/120	Negative
07	41	W	M	Not known	Not known	−35/120	Negative
08	35	B	F	Non-smoker	No response	−23/30	Negative
09	41	W	F	Non-smoker	Asthma/SOB/wheezing	−21/180	Negative
10	39	W	F	Non-smoker	Wheezing	−21/60	Negative
11	27	B	F	Non-smoker	Cough	−20/60	Negative
12	32	B	F	Non-smoker	Asthma/SOB/wheezing/conjunctivitis	−32/165	Negative
13	43	B	F	Smoker	No response	−27/240	Negative
14	35	W	F	Ex-smoker	Asthma/SOB/wheezing	−46/180	Negative
15	44	W	F	Non-smoker	Asthma/SOB/wheezing/nasal symptom/scratchy throat/eyes burn	−23/90	Negative
16	39	W	F	Non-smoker	Asthma/SOB/wheezing/conjunctivitis	−23/180	Negative
17	20	W	F	Non-smoker	Asthma/SOB/wheezing/nasal sympt/conjunctivitis	−34/90	Negative
18	34	B	M	Ex-smoker	No response	−26/90	Negative
19	25	W	M	Ex-smoker	Asthma/SOB/wheezing/nasal sympt/eczema/conjunctivitis/headache	−22/150	Negative
20	23	B	F	Not known	Asthma/SOB/wheezing	−22/120	Negative
21	32	B	F	Non-smoker	Asthma/SOB/wheezing	−26/90	−25/210
22	28	W	F	Non-smoker	Asthma/SOB/wheezing/eczema/hives	−20/210	−40/180
23	49	B	M	Smoker	Asthma/SOB/wheezing/conjunctivitis	−23/120	−35/90
24	19	W	F	Ex-smoker	Asthma/SOB/wheezing/conjunctivitis	−60/30	−26/30
25	60	W	F	Ex-smoker	Asthma/SOB/wheezing	−39/7	−22/12
26	32	B	M	Non-smoker	SOB/wheezing/nasal symptoms/conjunctivitis	−23/210	−37/210
Summary	36[c]	B/W 13/13	M/F 06/20	Smoker=2 Non-smoker=14 Ex-smoker=7	Asthma=17 Wheezing=18 SOB=18 Other=12	−28/124	−30/174

[a]a reactor had a 20% or greater drop in FEV_1 upon SS-ETS exposure. [b]drop in FEV_1/length of time to occur. [c]mean.

Table 3 Non-pulmonary symptoms reported by asthmatic and non-asthmatic subjects following SS-ETS exposure

Symptoms	Non-asthmatic non-reactors n=28	Asthmatic non-reactors n=104	Asthmatic reactors Sham (−) n=20	Asthmatic reactors Sham (−) n=6
Odor				
None-slight	1/8 (12.5)[1]	29/93 (31.2)	3/17 (17.6)	0/4 (0)
Moderate-severe	7/8 (87.5)	64/93 (68.8)	13/17 (76.5)	4/4 (100)
Nasal				
None-slight	3/7 (42.9)	27/97 (27.8)	4/17 (23.5)	1/4 (25)
Moderate-severe	4/7 (57.1)	70/97 (72.2)	12/17 (70.6)	3/4 (75)
Conjunctival				
None-slight	1/8 (12.5)	21/97 (21.6)	3/17 (17.6)	0/4 (0)
Moderate-severe	7/8 (87.5)	76/97 (78.4)	13/17 (76.5)	4/4 (100)
Pharyngeal				
None-slight	4/8 (50)	36/95 (37.9)	5/17 (29.4)	1/4 (25)
Moderate-severe	4/8 (50)	59/95 (62.1)	11/17 (64.7)	3/4 (75)
Annoyance				
None-slight	1/8 (12.5)	21/96 (21.9)	3/15 (20)	0/4 (0)
Moderate-severe	7/8 (87.5)	75/96 (78.1)	11/15 (73.3)	4/4 (100)

[1]Number reactors/total responders (percent).

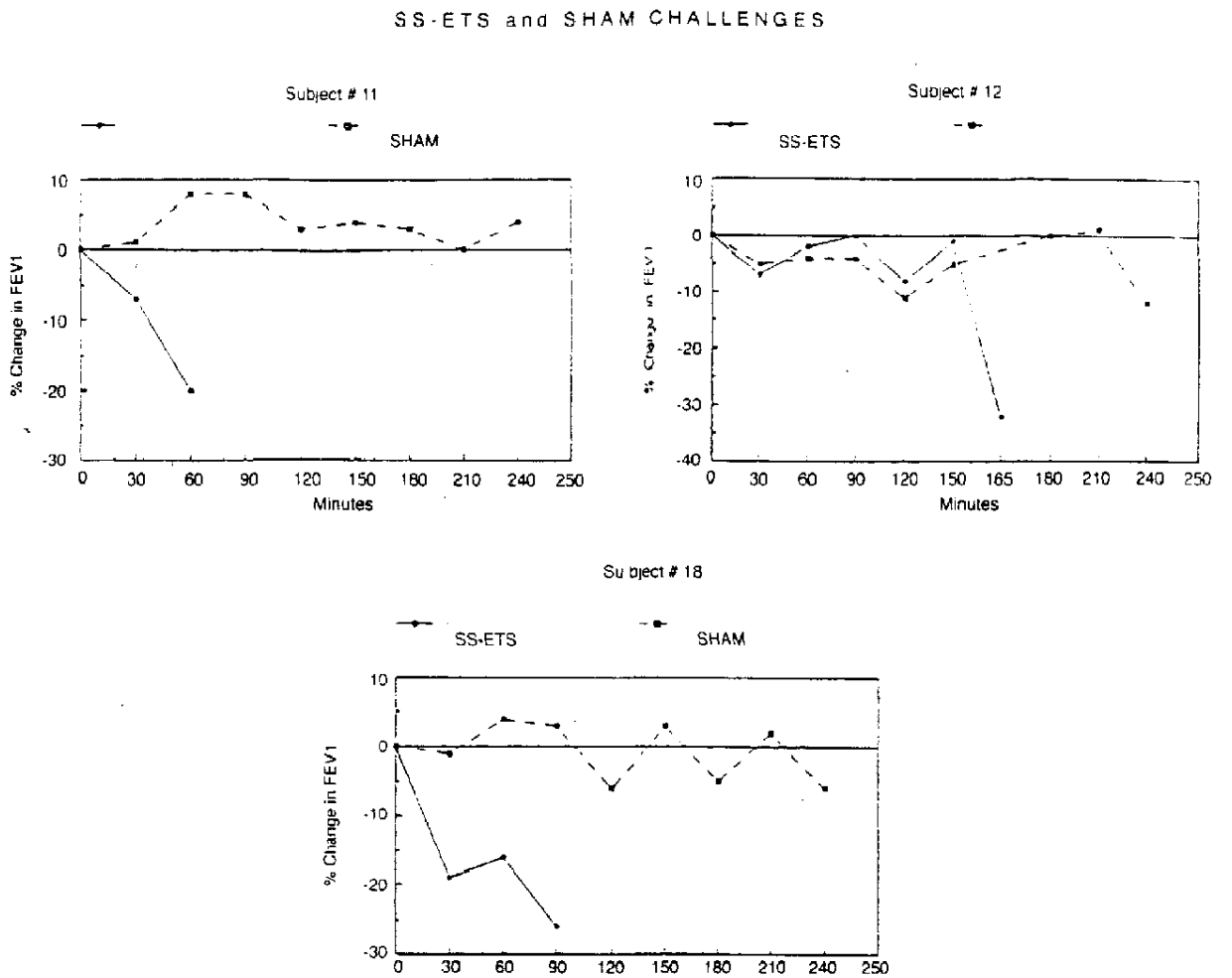

Fig. 1. Pulmonary responses of sham negative asthmatics to SS-ETS as measured by drop in FEV_1. The changes in lung function of three asthmatic subjects to SS-ETS are shown in this figure. All three asthmatics had negative sham challenges, indicating the specificity of their response to ETS.

self evaluation of lung functions following completion of a challenge.

Results

Study Population

A total of 130 asthmatics participated in the study (Table 1). They ranged in ages from 18 to 60 years (37 males, 93 females; 65 blacks, 65 whites). Eighty-six percent of the subjects were atopic. Fifty-one of the subjects were on inhaled $beta_2$ agonist inhalers, 60 were on theophylline, 22 were on inhaled steroids, 4 were on nasal steroids, 21 in the past had been on oral steroids, 6 were on cromolyn sodium, and 30 were on antihistamines and/or oral sympathomimetic agents. Medications were withheld for 24 hours prior to the challenge. Antihistamines were withheld for 48 to 72 hours. Fifty-five percent of the study subjects reported that they were exposed to ETS at home or at work.

Twenty-eight non-asthmatic subjects served as controls (Table 1). Of the total study population (158), 111 subjects never smoked while 30 were ex-smokers for at least 4 years.

Reactors to SS-ETS

While none of the 28 non-asthmatic controls reacted, with bronchospasm, 26 (20%) of the asthmatics demonstrated a significant (≥20% decrease in FEV_1) decline in their lung functions upon smoke exposure (Table 2). Most of these subjects reacted between 90 to 120 minutes of exposure; mean reaction time was 126 minutes. In order to determine the specificity of reactivity, all reactors were subjected to a control challenge, which was a sham challenge performed under identical con-

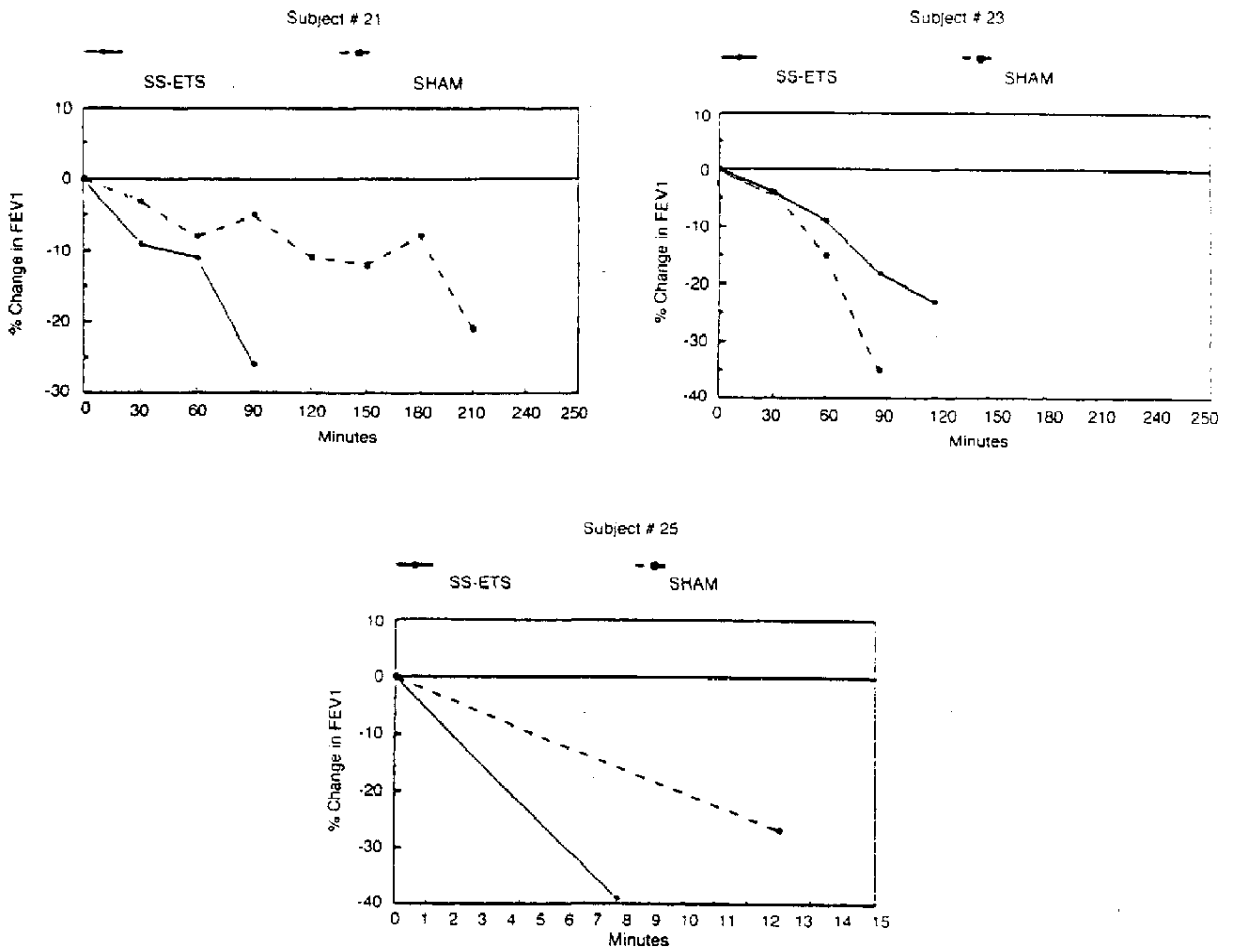

Fig. 2. Pulmonary responses of sham positive asthmatics to SS-ETS as measured by drop in FEV_1. These asthmatic subjects demonstrated positive lung function responses in both the SS-ETS and sham challenges, indicating that their responses to ETS are not specific.

ditions as for the ETS challenge, but without exposure to SS-ETS. Six of the 26 reactors had a positive sham challenge, whereas 20 had a negative sham response (Table 2). Examples of responses of reactors with negative and positive sham challenges are shown in Figures 1 and 2. Sham positive reactors were not distinguishable from sham negative reactors or reactors from non-reactors by chi-square analysis.

Non-pulmonary Symptoms

The responses of the various study groups in terms of development of non-pulmonary symptoms are summarized in Table 3. These results indicate that in all study groups, a substantial percentage of individuals reported nasal, conjunctival, or pharyngeal irritant symptoms following smoke exposure. Perceived smoke allergy was significantly different when asthmatics were compared to non-asthmatics ($P<0.001$) or ETS reactor asthmatics were compared to ETS non-reactor asthmatics ($P=0.037$, one tailed test). No other significant differences were noted. Furthermore, no relationship was detected between non-pulmonary symptoms and the subjects' own perceived smoke "allergy" (Table 4).

Table 4 Relationship of perceived smoke allergy to non-pulmonary symptoms

Perceived smoke allergy	Asthmatics			Controls (non-asthmatics) n=19
	ETS (−) n=79	ETS (+) Sham (−) n=14	ETS (−) Sham (+) n=6	
Yes	59 (75%)	13 (93%)	6 (100%)	7 (37%)
No	20 (25%)	1 (7%)	0 (0%)	12 (63%)

Table 5 Characterization of smoke challenge atmospheres

	Cigarette smoke concentrations			
	I	II	III	IV
Target smoke levels	800 cpm	400 cpm	200 cpm	100 cpm
Smoke index (cig – min/m^3)	1.18	0.59	0.27	0.128
Aerosol (cpm)	738±30	340±17	128±7	120±1
UVPM (μg/m^3)	1553±53	621±36	337±4	121±24
Nicotine (μg/m^3)	379±13	216±7	148±7	63±6
Carbon monoxide (ppm)	12.4	7.8	6	0.8

Table 6 Responses of smoke reactors to diminishing levels of ETS

Subject	1.18[1]	0.59	0.27	0.128
1	−24/180[2]	Negative		
2	−30/90	Negative		
3	−20/240	Negative		
4	−21/30	−24/180	Negative	
5	−20/150	−41/150	−41/90	Negative
6	−37/120	−22/30	−33/210	−38/180
7	−35/120	−24/180	−20/90	−22/90

[1]SS-ETS, smoke index – number of cigarettes continuously smoked – dilution flow rate. [2]% FEV_1 drop/minutes.

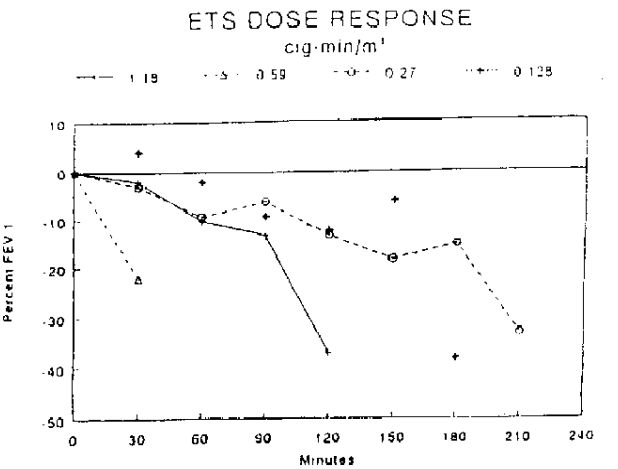

Fig. 3. SS-ETS dose response for subject 6. Subject 6 was exposed to target SS-ETS levels of 800 cpm (1.18 cig-min/m^3), 400 cpm (0.59 cig-min/m^3), 200 cpm (0.27 cig-min/m^3) and 100 cpm (0.128 cig-min/m^3). Results demonstrated a significant change in lung function after exposure to ETS levels as low as 100 cpm. There was no correlation of level of ETS exposure with length of response time.

Reactors' Responses to Diminishing ETS Levels

Seven selected positive SS-ETS reactors (negative sham responses) were exposed for up to 4 hours to decreasing levels of SS-ETS (Table 5). The results, summarized in Table 6, indicate that 4 of the 7 SS-ETS asthmatic reactors reacted with a significant drop in FEV_1 to levels of smoke less than 1.18 cigarette – min/m^3. Two subjects reacted to SS-ETS levels as low as 0.128 cigarette – min/m^3, suggesting that these individuals are exquisitely sensitive to ETS. Lower levels of smoke exposure were difficult to test since they approached background particulate levels in the ambient atmosphere. There does not appear to be a consistent relationship between diminishing levels of smoke exposure and reaction time in the individuals tested. The response of one subject (number 6) to diminished levels of SS-ETS is summarized in Figure 3.

Discussion

There is a plethora of information regarding the health effects of active smoking. As such, the effects of cigarette smoke, not only on smokers but also on their non-smoking co-workers and family members, is becoming a major medical and legal issue in the United States. There has been much attention recently to epidemiological assessments of potential chronic health effects, especially cancer, in non-smokers exposed to ETS. In spite of this, there is little information available on the acute effects of smoke on the non-smoking population or the levels which can cause acute adverse reactions. This is critical in that many municipalities have banned smoking, not only in public places but also in office buildings, restaurants, and stadiums. Thus, there is a need to obtain more information about the effects of ETS exposure in real-life situations, and the levels of smoke that may cause these acute effects.

Our study has chosen to investigate the respiratory effects of ETS in non-smoking asthmatic subjects. Our experience suggests that the majority of asthmatics believe that their asthma is worse following smoke exposure, and many consider themselves allergic to ETS. However, the results of this study do not support this. Only 20% of the asthmatic group studied showed significant changes in FEV_1 upon exposure to ETS and 23% of these reacted non-specifically. Why do such a large number of asthmatics complain of smoke-induced symptoms, yet only approximately 15% appear to have significant lung function changes in response to smoke challenge? If asthmatics exposed to ETS have a drop in their FEV_1 of less than 20%, one explanation may be that these asthmatics have a decline in small airways function not detected by measuring FEV_1. Thus, if these asthmatics with changes in both large and small airways function upon smoke exposure are considered, the percentage of responders would be much higher. However, the mean drop in FEV_1 of non-responder asthmatics is no less than 1% after 240 minutes of challenge, suggesting that this is not the case.

Another explanation is that other effects reported by asthmatics such as eye, nose, and throat irritation are the basis for the substantial numbers of asthmatics who report difficulties when encountering ETS.

Finally, the issue could be raised that there is variability in ETS reactivity and that a larger number of reactors may have been detected by multiple ETS exposures. Certainly, we cannot exclude this possibility in the current study since multiple challenges were beyond the scope of this investigation. However, a previous investigation with a static smoke inahalation challange chamber (Menon et al., 1991) demonstrated that 24 months following the initial challenge, 5 out of 6 reactors remained reactive and all 9 non-reactors remained non-reactive to environmental tobacco smoke. Thus, we consider any substantial change in tobacco smoke reactivity unlikely as a variable affecting our results.

Interestingly, the responses to ETS do not appear to resemble the dynamics of either an immediate or late-phase allergic reaction. Generally, most subjects responded to ETS 90 to 120 minutes following ETS initiation exposure. This is much later than the immediate type IgE mediated reaction, but certainly earlier than a classical late allergic asthmatic reaction. The response to smoke generally is a gradual decrease in FEV_1 which occurs over time. In contrast, one subject demonstrated an immediate type reaction to ETS within 10 minutes of exposure but also had a similar response during sham challenge, possibly demonstrating a psychological response.

What mechanisms cause ETS-induced lung function changes? Although there have been reports in the early 70's and 80's that suggest that a substantial number of atopics have positive skin test reactions to tobacco leaf extracts, we have demonstrated that these skin responses do not correlate with pulmonary reactivity to smoke (Lehrer et al., 1986). Clearly, our current results, as well as earlier studies (Stankus et al., 1988; Menon et al., 1988; Lehrer et al., 1986), suggest that this is not due to a classical IgE mediated allergic reaction. More than likely, there is no classical IgE-mediated reaction to smoke which causes an allergic reaction, at least for the vast majority of ETS responders. Nevertheless, most asthmatics who believe that they have smoke allergy also report significantly higher non-pulmonary symptoms to smoke exposure. Probably ETS-induced respiratory responses represent a sensory-neural irritant response of the bronchial tract. Indeed, studies by Musmand and colleagues (Musmand et al., 1993a; 1993b) from our laboratory have suggested that the release of certain neuropeptides in nasal lavage fluids of subjects exposed to ETS would be in agreement of this hypothesis.

The fact that almost 25% of our ETS responders have positive sham responses is an interesting finding (Lehrer et al., 1993). Perhaps some subjects develop broncho-constriction from medication withdrawal or from psychological responses as discussed above. This emphasizes the need for proper controls and more critical analysis of data when exposing individuals to ETS. This is particularly a problem with not only ETS, but with other noxious substances that have a unique odor in which a completely blinded challenge is virtually impossible. In view of this reality, it is always important to have proper controls.

Interestingly, some individuals are exquisitely sensitive to ETS in that they respond to levels of tobacco smoke that are much lower than those found in bars and stadiums and similar to those found in the homes of some smokers (Ogden and Maiolo, 1989). Our protocol provides a means for measuring the sensitivity of such individuals who may complain of very low levels of ETS exposure and must be taken into account whenever regulations governing levels of ETS in public places are formulated.

Smoking and the effects of ETS on non-smokers continue to remain exceedingly complex and important issues confronting modern society. It is likely that smoking and ETS exposure will continue to be public health concerns for some time. Therefore, we need further studies assessing the effects of ETS on non-smokers, as well as more precise methods for analyzing the levels of ETS affecting these individuals. It is only through valid scientific observation and rational discussion of results from such studies that the issues surrounding ETS exposure can be determined adequately and fairly.

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